

**AMENDMENTS TO THE SPECIFICATION:**

Pursuant to the revised 37 § CFR 1.121, please amend the specification as follows:

Please replace the paragraph beginning at page 11, line 3 with the following amended paragraph:

C1 A "recombinant polynucleotide" or a "recombinant polypeptide" is a non-naturally occurring polynucleotide or polypeptide that includes nucleic acid or amino acid sequences, respectively, from more than one source nucleic acid or polypeptide, which source nucleic acid or polypeptide can be a naturally occurring nucleic acid or polypeptide, or can itself have been subjected to mutagenesis or other type of modification. The source polynucleotides or polypeptides from which the different nucleic acid or amino acid sequences are derived are sometimes homologous (*i.e.*, have, or encode a polypeptide that **encodes** has, the same or a similar structure and/or function), and are often from different isolates, serotypes, strains, species, of organism or from different disease states, for example.

Please replace the paragraph beginning at page 12, line 8 with the following amended paragraph:

C2 One example of an algorithm that is suitable for determining percent sequence identity and sequence similarity is the BLAST algorithm, which is described in Altschul *et al.*, *J. Mol. Biol.* 215:403-410 (1990). Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information and its website (~~<http://www.ncbi.nlm.nih.gov/>~~). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul *et al.*, *supra*). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are then extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0)

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and N (penalty score for mismatching residues; always  $< 0$ ). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, an expectation (E) of 10, a cutoff of 100,  $M=5$ ,  $N=-4$ , and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength (W) of 3, an expectation (E) of 10, and the BLOSUM62 scoring matrix (*see Henikoff & Henikoff (1989) Proc. Natl. Acad. Sci. USA 89:10915*).

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Please replace the paragraph beginning at page 16, line 14 with the following  
amended paragraph:

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A "subsequence" refers to a sequence of nucleic acids or amino acids that **comprise** comprises a part of a longer sequence of nucleic acids or amino acids (*e.g.*, polypeptide) respectively.

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Please replace the paragraph beginning at page 18, line 17 with the following  
amended paragraph:

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Exemplary formats and examples for sequence recombination, sometimes referred to as DNA shuffling, evolution, or molecular breeding, have been described by the present inventors and co-workers in co-pending applications U.S. Patent Application Serial No. 08/198,431, filed February 17, 1994, now U.S. Patent No. 5,605,793; Serial No. PCT/US95/02126, filed [ ] February 17, 1995[ ]; Serial No. 08/425,684, filed April 18, 1995, now U.S. Patent No. 5,834,252; Serial No. 08/537,874, filed October 30, 1995, now U.S. Patent No. 5,830,721; Serial No. 08/564,955, filed November 30, 1995, now U.S. Patent No. 5,811,238; Serial No. 08/621,859, filed March 25, 1996, now U.S. Patent No. 6,117,679; Serial No. 08/621,430, filed March 25, 1996, now abandoned; Serial No. PCT/US96/05480, filed April 18, 1996[ ]; Serial No. 08/650,400, filed May 20, 1996, now U.S. Patent No. 5,837,458; Serial No. 08/675,502, filed July 3, 1996, now U.S. Patent No. 5,928,905;

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Serial No. 08/721,824, filed September 27, 1996, which was converted to provisional U.S. App. Serial No. 60/037,742, now abandoned; Serial No. PCT/US97/17300, filed September 26, 1997; and Serial No. PCT/US97/24239, filed December 17, 1997; Stemmer, Science 270:1510 (1995); Stemmer et al., Gene 164:49-53 (1995); Stemmer, Bio/Technology 13:549-553 (1995); Stemmer, Proc. Natl. Acad. Sci. U.S.A. 91:10747-10751 (1994); Stemmer, Nature 370:389-391 (1994); Cramer et al., Nature Medicine 2(1):1-3 (1996); Cramer et al., Nature Biotechnology 14:315-319 (1996), each of which is incorporated by reference in its entirety for all purposes.

Please replace the paragraph beginning at page 60, line 18 with the following amended paragraph:

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In presently preferred embodiments, the reagents obtained using the invention are used in conjunction with a genetic vaccine vector. The choice of vector and components can also be optimized for the particular purpose of treating allergy or other conditions. For example, an antigen associated with treating a particular condition can be optimized using recombination and selection methods analogous to those described herein. Such methods, and antigens appropriate for various conditions, are described in copending, commonly assigned US Patent Application Serial No. 09/247,890, now U.S. Patent No. 6,541,011, [[\_\_\_\_\_,]] entitled "Antigen Library Immunization," which was filed on February 10, 1999 as TTC Attorney Docket No. 18097-028710US. The polynucleotide that encodes the recombinant antigenic polypeptide can be placed under the control of a promoter, *e.g.*, a high activity or tissue-specific promoter. The promoter used to express the antigenic polypeptide can itself be optimized using recombination and selection methods analogous to those described herein, as described in International Application No. PCT/US97/17300 (International Publication No. WO 98/13487). The reagents obtained using the methods of the invention can also be used in conjunction with multicomponent genetic vaccines, which are capable of tailoring an immune response as is most appropriate to achieve a desired effect (*see, e.g.*, copending, commonly assigned US Patent Application Serial No. 09/247,888, now abandoned, [[\_\_\_\_\_,]] entitled "Genetic Vaccine Vector Engineering," filed on February 10, 1999 as TTC Attorney Docket No. 18097-030100US). It is sometimes advantageous to employ a genetic vaccine that is targeted for a particular target cell type (*e.g.*, an antigen presenting cell or an

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antigen processing cell); suitable targeting methods are described in copending, commonly assigned  
US Patent Application ~~patent application~~ Serial No. 09/247,886 [[\_\_\_\_\_]] entitled "Targeting  
of Genetic Vaccine Vectors," filed on February 10, 1999 as TTC Attorney Docket No. 18097-  
030200US.

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